

**PATENT**

**Attorney Docket No.06854.0046**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of

Katsuyoshi Nagao et al.

Appln. No.: 10/554,094

Group Art Unit: 3761

Filed: October 21, 2005

Examiner: MARCETICH, ADAM M

For: DRUG SOLUTION FILLING PLASTIC AMPOULE AND PROCESS FOR PRODUCING  
THE SAME

Commissioner for Patents

P.O. Box 1450

Alexandria, Virginia 22313-1450

Sir:

Declaration Under 37 C.F.R. §1.132  
U.S. Application No. 10/554,094

**DECLARATION UNDER 37 C.F.R. § 1.132**

I, Yuki MANABE, hereby declare and state:

THAT I am a citizen of Japan;

THAT I received Master's degree from Tokushima University in 1996;

THAT I was employed by Otsuka Pharmaceutical Factory, Inc. of Naruto from 1996, ultimately holding the position of Supervisor of Pharmaceutical Technology Department, and that I engaged in the development and production of the DRUG SOLUTION FILLING PLASTIC AMPOULE AND PROCESS FOR PRODUCING THE SAME claimed in the present application;

THAT I am responsible for the research work related to the above-identified application;

THAT the following experiments were conducted by myself;

## EXPERIMENTS

The acronyms and properties of ingredients for the drug solution filling plastic ampoule are shown below.

### Polyolefins

- PE1: A copolymer of ethylene and 1-butene (having a density of  $0.92\text{g/cm}^3$  and a melt flow rate (MFR) of  $1.0\text{g}/10\text{min}$  (at  $190^\circ\text{C}$ ) and available under the trade name of ULTZEX 2010B from PRIME POLYMER Co.,Ltd.)
- PE4: A copolymer of ethylene and 1-butene (having a density of  $0.96\text{g/cm}^3$  and a melt flow rate (MFR) of  $15.0\text{g}/10\text{min}$  (at  $190^\circ\text{C}$ ) and available under the trade name of NEO-ZEX 65150B from PRIME POLYMER Co.,Ltd.)

### Polycycloolefin

- COC3 : A copolymer of ethylene and tetracyclododecene (having a specific gravity of 1.02, an MFR of  $15.0\text{g}/10\text{min}$  (at  $260^\circ\text{C}$ ) and a Tg of  $70^\circ\text{C}$  and available under the trade name of APEL APL8008T from Mitsui Chemicals Inc.)

### Experiment 1

With the use of a blow-fill-seal machine having a triple layer blow die, a drug solution filling plastic ampoule of a triple layer structure (having a volume of 5mL) including an inner layer of PE1 (polyolefin), an intermediate layer of blends of COC3 (polycycloolefin) and PE4 (polyolefin) in a weight ratio of 80:20 and an outer layer of PE1 and filled with 5mL of a 0.005%

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nitroglycerine aqueous solution was produced. The inner layer, the intermediate layer and the outer layer of the ampoule had thicknesses of 50 $\mu$ m, 100 $\mu$ m and 500 $\mu$ m, respectively.

#### Comparative Experiment 1

A drug solution filling plastic ampoule of a triple layer structure was produced in substantially the same manner as in Experiment 1, except that COC3 only was used as the plastic material for the intermediate layer instead of blends of COC3 (polycycloolefin) and PE4 (polyolefin).

#### Evaluation of external quality of the plastic ampoules

The plastic ampoules produced in Experiments 1 and Comparative Experiment 1 were taken of a picture with the digital camera, respectively. Two pictures are shown in Fig. 1 and 2, respectively.

The plastic ampoule shown in Fig. 1 has smooth surface and excellent external quality. On the other hand, the plastic ampoule shown in Fig. 2 has rough surface and inferior external quality in comparison to the one of Experiment 1.

That is, a plastic ampoule with excellent external quality can be produced by using blends of polycycloolefin and polyolefin as the plastic material for the intermediate layer.

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I, the undersigned, declare that all statement made herein on my knowledge are true and that all statements made on information and belief are believed to be true: and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and such willful false statements may jeopardize the validity of the application or any issuing thereon.

Signed this 29 day of August 2008.

Yuki Manabe

Yuki MANABE